INTRODUCTION
Phenolic compounds have been widely studied as potential therapeutic agents. For instance, rutin and phenolic acids, such as, ferulic, caffeic and p-coumaric acids have several interesting properties, including anticancer activity. Nonetheless, the impact of these phenolic compounds on renal cancer is not established and better understanding this matter remains essential. Furthermore, despite the potential applicability of these compounds, their low solubility may be an obstacle for their applicability. In this context, the use of ionic liquids (ILs) may be a valuable tactic to surpass this impasse. Thus, the aim of this work was to evaluate the impact of rutin and ferulic, caffeic and p-coumaric acids and of the ILs on the viability of renal cancer cells, as well as the influence of the studied ILs on the solubility and cytotoxicity of rutin, while considering safety.

MATERIAL AND METHODS
Ionic liquid synthesis: The ILs, (2-hydroxyethyl) trimethylammonium-L-phenylalaninate, [Chol][Phe], and 2-hydroxyethyl-trimethylammonium glycinate [Chol][Gly] were prepared according to the literature.

Cell viability assay: the influence of the phenolic compounds and of the ILs on cell viability was evaluated in 786-O human renal cancer cells and the influence of rutin and the ILs on cell viability were also evaluated in normal kidney Vero cells using the MTT assay.

Solubility studies: rutin saturated solutions in water or in water:IL mixtures were prepared at 25 °C for 72h (n=3).

Cell DNA content analysis: the effect of rutin and of the studied ILs on 786-O cell cycle was analysed by assessing the cell DNA content, according to the literature.

RESULTS AND DISCUSSION
Cell viability
The MTT assay results showed that the phenolic acids (up to 250 µM; 48 h) did not induced cytotoxic effects on 786-O cells (Fig.1A-C). Only rutin presented cytotoxicity (Fig.1D) and in consequence was further studied.

Viability studies of the [Chol][Phe] and [Chol][Gly] ILs were performed in Vero cells and results showed that the upper concentrations of these ILs should be 0.3 % and 0.2 %, respectively, to ensure safety in further studies (Fig.2A).

Rutin induced a concentration-dependent decrease on cell viability in both cell lines, being most pronounced in 786-O cells (Fig.2B-C).

The presence of the ILs did not significantly influence the cytotoxic profile of rutin, in both cell lines.

Solubility studies
The presence of 0.3 % of [Chol][Phe] and 0.2 % of [Chol][Gly] ILs allowed a 13-fold and 9-fold increase on rutin’s solubility, respectively.

Cell cycle progression
Exposure to rutin (50 µM) caused an increase in sub-G1 population of 786-O cells (Fig.3).

The co-treatment of rutin with ILs did not significantly changed the 786-O cells cycle progression, when compared with rutin exposed cells.

CONCLUSION
Rutin showed a potential anticancer effect since revealed higher cytotoxicity in 786-O renal cancer cells than in non-tumor Vero kidney cells.

At non-toxic concentrations, ILs enhanced rutin’s solubility and did not interfere with the impact of rutin on the renal cells. Hence, choline-based ILs may act as functional excipients for the delivery of this poorly soluble compound with therapeutic potential on renal cancer.

REFERENCES